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EXAMINER	
DEVI, SARVAMANGALA J N	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 05/09/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/608,873	FLETCHER, HANSEL M.	
	Examiner	Art Unit	
	S. Devi, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RESPONSE TO APPLICANT'S AMENDMENT

Applicant's Amendment

1) Acknowledgment is made of Applicant's amendment filed 12/08/04 in response to the non-final Office Action mailed 06/09/04. With this, Applicant has amended the specification.

Status of Claims

2) Claims 1 and 2 have been canceled via the amendment filed 12/08/04.

Claims 3, 6-8 and 10 have been amended via the amendment filed 12/08/04.

Claims 3-10 are pending and are under examination.

Terminal Disclaimer

3) Acknowledgment is made of Applicant's submission of a terminal disclaimer filed 12/08/04 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of US patents 6,254,863 and US 6,585,977.

Prior Citation of Title 35 Sections

4) The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

Prior Citation of References

5) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

Objection(s) Withdrawn

6) The objection to the title made in paragraph 5 of the Office Action mailed 06/09/04 is withdrawn in light of Applicants' amendment to the title.

7) The objection to the specification made in paragraph 6 of the Office Action mailed 06/09/04 is withdrawn in light of Applicants' amendments to the specification.

Rejection(s) Withdrawn

8) The rejection of claims 3-6 and 7-10 made in paragraph 8 of the Office Action mailed 06/09/04 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4 and claims 5-8 of the U.S. Patent 6,254,863 ('863), is withdrawn in light of Applicant's submission of a terminal disclaimer disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of the US patent 6,254,863.

9) The rejection of claims 3-10 made in paragraph 9 of the Office Action mailed 06/09/04 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4 of the U.S. Patent 6,585,977 ('977), is withdrawn in light of Applicant's submission of a terminal disclaimer disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of the US patent 6,585,977.

10) The rejection of claims 3-10 made in paragraph 10 of the Office Action mailed 06/09/04 under 35 U.S.C § 112, first paragraph, as being non-enabling, with regard to the deposit issue, is withdrawn in light of Applicant's deletion of the limitation reciting the specifically deposited strain.

11) The rejection of claims 3-6 made in paragraph 11 of the Office Action mailed 06/09/04 under 35 U.S.C § 112, first paragraph, as being non-enabling with regard to the scope, is withdrawn in light of Applicant's amendment to the base claim.

12) The rejection of claim 3 made in paragraph 13(a) of the Office Action mailed 06/09/04 under 35 U.S.C. § 112, second paragraph as being indefinite, is withdrawn in light of Applicant's amendment to the claim.

13) The rejection of claim 7 made in paragraph 13(b) of the Office Action mailed 06/09/04 under 35 U.S.C. § 112, second paragraph as being indefinite, is withdrawn in light of Applicant's amendment to the claim.

14) The rejection of claim 6 made in paragraph 13(c) of the Office Action mailed 06/09/04

under 35 U.S.C. § 112, second paragraph as being indefinite, is withdrawn in light of Applicant's amendment to the claim.

15) The rejection of claim 8 made in paragraph 13(d) of the Office Action mailed 06/09/04 under 35 U.S.C. § 112, second paragraph as being indefinite, is withdrawn in light of Applicant's amendment to the claim.

16) The rejection of claims 5, 6 and 8-10 made in paragraph 13(f) of the Office Action mailed 06/09/04 under 35 U.S.C. § 112, second paragraph as being indefinite, is withdrawn in light of Applicant's amendment to the base claim.

Rejection(s) Maintained

17) The rejection of claim 10 made in paragraph 13(e) of the Office Action mailed 06/09/04 under 35 U.S.C. § 112, second paragraph as being indefinite, is maintained for reasons set forth therein.

18) The rejection of claims 7-10 made in paragraph 11 of the Office Action mailed 06/09/04 under 35 U.S.C § 112, first paragraph, as being non-enabling with regard to the scope, is maintained for reasons set forth therein and herebelow.

Applicant contends that claim 3 has been amended to incorporate the limitation of claim 1. Applicant states that claim 3 does not claim that 'the method [comprises] administering to the mammal at least one dose of the mutant of *recA* defective mutant of *Porphyromonas gingivalis*', but instead claims that 'the method [comprises] administering to the mammal at least one dose of the mutant of a NON-VIRULENT, *recA* defective mutant of *Porphyromonas gingivalis*' [Emphasis in original]. Applicant submits that the bacteria is not merely *recA* defective, but it is also 'non-virulent' that is critical to the present invention. Applicant asserts that the teaching in the present disclosure is sufficient to teach one of ordinary skill in the art to select any non-virulent, *recA* defective mutant of *Porphyromonas gingivalis* for use in the claimed invention. Applicant further opines that not to allow claim 3 as presently written would be to impermissibly limit the invention to a preferred embodiment. Applicant concludes that he has provided detailed instructions to one of ordinary skill in the art to create a useful mutant for the presently claimed

invention, but is not required to teach how to create all possible such mutants.

Applicant's arguments have been carefully considered, but are non-persuasive. It is noted that Applicant has not advanced any specific arguments with regard to the rejection of claims 7-10. Contrary to Applicant's assertion, the method that uses the deposited non-virulent *recA* defective mutant of *Porphyromonas gingivalis* is not just the preferred embodiment, but the only enabled embodiment. Of the four species of *recA* defective mutant of *Porphyromonas gingivalis* produced within the instant specification, three species of *recA* defective mutants of *Porphyromonas gingivalis*, FLL33, FLL34 and FLL35, did not turn out to be non-virulent mutants. Instead, these mutant species remained virulent. One of skill in the art would not expect these virulent species to decrease the growth rate or reproduction rate of wild-type *Porphyromonas gingivalis*. One mutant species, FLL32, that is enabled as a non-virulent species is deposited at the ATCC under the accession number 202109. This FLL32 mutant was used for administration to a mammal. However, there is no evidence showing that the administration of this FLL32 mutant to a mammal, let alone a human, did indeed result in the decreased growth and reproduction rates of a non-virulent or wild type *Porphyromonas gingivalis*, before or after the administration of the *recA* defective mutant *Porphyromonas gingivalis*. The growth or reproduction rate of a wild-type mutant or non-mutant *Porphyromonas gingivalis* was not measured or quantified either before or after the administration of the *recA* mutant of *Porphyromonas gingivalis* to a mammal, including a human. For the *recA* defective mutant genus recited in the instant claims to be enabled, a representative number of *recA* defective mutant species must be shown to be non-virulent while having the ability to decrease growth and reproduction rates of a wild-type *Porphyromonas gingivalis* in a mammal, particularly in view of the art-recognized unpredictability and the unpredictability demonstrated by the Applicant within the instant specification. In applications directed to inventions in arts where the results are unpredictable, the disclosure of a single species usually does not provide an adequate basis to support generic claims. *In re Soll*, 97 F.2d 623, 624, 38 USPQ 189, 191 (CCPA 1938). In cases involving unpredictable factors, such as most chemical reactions and physiological activity, more

may be required. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) (contrasting mechanical and electrical elements with chemical reactions and physiological activity). See also *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); *In re Vaeck*, 947 F.2d 488, 496, 20 USPQ2d 1438, 1445 (Fed. Cir. 1991). This is because it is not obvious from the disclosure of one species, what other species will work. The rejection stands.

Rejection(s) under 35 U.S.C § 112, First Paragraph

New Matter

18) Claim 3 and those dependent therefrom are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claim 3, as amended, includes the limitation: the mutant of 'a non-virulent, *recA* defective mutant of *Porphyromonas gingivalis*'. Applicant states that the claim has been amended to include the limitation of claim 1. However, the canceled claim 1 was drawn to a 'non-virulent, *recA* defective mutant of *Porphyromonas gingivalis*', but not to 'the mutant of a non-virulent, *recA* defective mutant of *Porphyromonas gingivalis*', as recited currently. Therefore, the new limitation in the instant base claim is considered to be new matter. *In re Rasmussen*, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step from a method. See M.P.E.P. 608.04 to 608.04(c).

Applicant is invited to point to specific line and page numbers of the specification, as originally filed, that provide descriptive support for the limitation identified above, or to remove the new matter from the claim(s).

Lack of Enablement

19) Claim 3 and those dependent therefrom are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the

application was filed, had possession of the claimed invention. This is a lack of enablement rejection.

Instant claims are evaluated based on the *Wands* analysis. Many of the factors regarding undue experimentation have been summarized in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Circ. 1988) as follows:

- The quantity of experimentation necessary (time and expense);
- The amount of direction or guidance presented;
- The presence or absence of working examples of the invention;
- The nature of the invention;
- The state of the art;
- The relative skill of those in the art;
- The predictability or unpredictability of the art; and
- The breadth of the claims.

Instant claims are drawn to a method of decreasing the growth rate or reproduction rate of wild-type *Porphyromonas gingivalis* in a mammal, such as a human, by administering to the mammal at least one dose of 'the mutant of a non-virulent, *recA* defective mutant of *Porphyromonas gingivalis*'. Unlike the single mutant used in the method of claim 7, the mutant administered to the mammal in the method of claim 3 is a double mutant, i.e., a further mutant of the non-virulent, *recA* defective mutant of *Porphyromonas gingivalis*. However, the instant specification does not teach such a double mutant and its use in a method of decreasing the growth rate or reproduction rate of wild-type *Porphyromonas gingivalis* in a mammal, such as a human, by administering to the mammal at least one dose of the double mutant of *Porphyromonas gingivalis*. The instant specification does not provide disclosure and specific guidance as to how to produce a further mutant of a *recA* defective mutant of *Porphyromonas gingivalis* such that it has the ability to decrease the growth rate or reproduction rate of wild-type *Porphyromonas gingivalis* in any mammal, let alone a human. The instant specification lacks probative evidence enabling the claimed method.

The instant specification shows that the only non-virulent *recA* defective mutant of *Porphyromonas gingivalis* that has been produced in the instant specification is a single mutation-carrying FLL32, deposited at ATCC under the accession number 202109. A second mutant of

this mutant is not taught in the instant application. The precise type of mutation that should be carried out in an already *recA* mutated *Porphyromonas gingivalis* is not taught. The instant application does not provide any evidence showing that administration, to any mammal let alone a human, of the single mutant, i.e., the non-virulent FLL32 mutant, results in decreased growth and reproduction rates of a non-virulent or wild type *Porphyromonas gingivalis*, before or after administration of the *recA* defective mutant *Porphyromonas gingivalis*. A review of the specification shows that a reproducible construction of even a single *recA* defective mutant of *Porphyromonas gingivalis* such that it acquires the property of non-virulence and the ability to decrease the growth rate or reproduction rate of wild-type *Porphyromonas gingivalis* in any mammal, let alone a human, is an unpredictable event. The growth or reproduction rate of a virulent or non-virulent, a mutant or non-mutant *Porphyromonas gingivalis* has not been measured or quantified either before or after the administration of the *recA* mutant of *Porphyromonas gingivalis* to a mammal, including a human. Whether or not a non-virulent mutant of a bacterial strain decreases the growth or reproduction rate of a bacterium on administration to a mammal is unpredictable, since such an effect is also dependent on the host factors and the virulence or non-virulence and/or the degree of virulence of the challenging or infecting strain of *Porphyromonas gingivalis*. Furthermore, both the instant specification and the art recognize unpredictability in obtaining *recA* defective mutants of *Porphyromonas gingivalis* that are non-virulent. For instance, the instant specification describes the single-mutation carrying FLL32 strain of *Porphyromonas gingivalis* to be a *recA* defective mutant that lacked hemolytic activity on blood agar, lacked the proteolytic activity and lacked black pigmentation (see page 4, last full paragraph) and which exhibited substantially reduced virulence when introduced into mammals (see paragraph bridging pages 4 and 5). However, three other *recA* defective mutant strains of *Porphyromonas gingivalis* , FLL33, FLL34 and FLL35, displayed beta hemolytic activity and black pigmentation similar to the wild-type W83 (see page 9). For example, the FLL33 mutant showed more proteolytic activity than the wild-type W83 (see pages 9 and 10). The specification explicitly states that 'the inactivation of the *recA* gene in *Porphyromonas gingivalis* FLL33 did not significantly affect the virulence of *Porphyromonas gingivalis*', but the

'mutation in the FLL32 strain significantly affected the virulence of *Porphyromonas gingivalis*' (see page 15, last full paragraph). The art also taught that the wild-type W83 strain and the *recA* mutant FLL33 (i.e., a single mutant) showed the same level of virulence. See Fletcher HM. *In*: *Abstracts in Microbial Pathogenesis*, page 101, abstract B-424, Miami Beach, Florida, May 4-8, 1997 (Applicant's IDS) and Fletcher *et al. Infect. Immun.* 65: 4592-4597, 1997 (Applicant's IDS). The virulent FLL33 may also be FLL32, which has reverted back to the virulent phenotype due to the unstable *recA* mutation. It is unlikely that the now recited mutant of a *recA* defective mutant would have the ability to decrease the growth or reproduction rate of a wild-type or non-wild-type *Porphyromonas gingivalis*, absent evidence to the contrary. Due to the demonstrated unpredictability in producing even a single mutation-carrying *recA* defective mutant that is functional as recited, i.e., non-virulent with the ability to decrease the growth or reproduction rate of a wild-type or non-wild-type *Porphyromonas gingivalis*, there is absolutely no predictability that a second mutation in the *recA* defective mutant of *Porphyromonas gingivalis* would result in a mutant of the *recA* defective mutant that would decrease the growth rate or reproduction rate of wild-type *Porphyromonas gingivalis* in any mammal, let alone a human. No *in vivo* data from a mammal, or *in vitro* data correlative of *in vivo* decrease in the growth rate or reproduction rate of wild-type *Porphyromonas gingivalis* in a mammal, are provided. The instant claims are viewed as being non-enabled for reasons set forth above. Undue experimentation would have been required by one of skill in the art at the time of the effective filing date of the instant application to reproducibly practice the invention as claimed due to the lack of enabling disclosure, the lack of specific guidance, the lack of enabling working examples, the demonstrated unpredictability as described within the specification and as reflected in the state of the art, the breadth of claims and the quantity of experimentation necessary.

Rejection(s) under 35 U.S.C § 112, Second Paragraph

20) Claims 3-10 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant(s) regards as the invention.

(a) Claim 3 has improper antecedence in the limitation: '**the** mutant of a .....

Porphyromonas gingivalis' (see line 3), because there is no earlier recitation of a 'mutant' in the claim.

(b) Claim 5 is confusing in the limitation: 'method of claim 3, wherein ..... the non-virulent, *recA* defective mutant of *Porphyromonas gingivalis*'. Claim 5 depends from claim 3, which does not recite 'a non-virulent, *recA* defective mutant of *Porphyromonas gingivalis*', but recites 'the mutant of a non-virulent, *recA* defective mutant of *Porphyromonas gingivalis*'. A 'mutant' and 'a mutant of a mutant' are two different products of differing scope.

(c) Claim 6 is indefinite and confusing in the limitation: 'the mutant of *Porphyromonas gingivalis*', because it is unclear which mutant of claim 3 does this limitation encompass. Claim 6 depends from claim 3, which recites a '*recA* defective mutant of *Porphyromonas gingivalis*' and 'the mutant of a non-virulent, *recA* defective mutant of *Porphyromonas gingivalis*'.

(d) Claim 6 is further confusing with regard to the antecedence of the limitation: 'wherein the dose' (see line 1) which is inconsistent with the limitation: 'wherein .... the at least one dose' in line 2 of claim 5. For clarity, proper antecedence and consistency, it is suggested that Applicant replace the limitation with --wherein the at least one dose--.

(e) Analogous criticism applies to claim 10 with regard to the limitation 'the dose' in line 3 of the claim.

(f) Claims 9 and 10 lack proper antecedent basis in the limitation: 'a non-virulent, *recA* defective mutant of *Porphyromonas gingivalis*'. Claims 9 and 10 depend from claim 7, which already recites 'a non-virulent, *recA* defective mutant of *Porphyromonas gingivalis*'. Therefore, for proper antecedence, it is suggested that Applicant replace the limitation with --the non-virulent, *recA* defective mutant of *Porphyromonas gingivalis*'--.

(g) Claims 4-6 and 8-10, which depend from claims 3 and 7 respectively, are also rejected as being indefinite, because of the indefiniteness identified above in the base claim.

Remarks

21) Claims 3-10 stand rejected.

22) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile

transmission. Papers should be transmitted via the PTO Fax Center, which receives transmissions 24 hours a day and 7 days a week. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The central Fax number for submission of amendments, responses or papers is (703) 872-9306.

23) Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAG or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.Mov. Should you have questions on access to the Private PAA system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

24) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (571) 272-0864.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

May, 2005

S. DEVI, PH.D.
PRIMARY EXAMINER